Cyanation of Iodobenzene Catalyzed by Pd (dba) • CHCl (Commemoration Issue Dedicated to Professor Shinzaburo OKA On the Occasion of His Retirement)

AUTHOR(S):

Takagi, Kanetaro

Bull. Inst. Chem. Res., Kyoto Univ., Vol. 67, No. 3, 1989

Note

Cyanation of Iodobenzene Catalyzed by $Pd_2(dba)_3 \cdot CHCl_3$

Kentaro TAKAGI

Received August 1, 1989

The catalytic ability of $Pd_2(dba)_3 \cdot CHCl_3$ in a nucleophilic displacement of iodobenzene with cyanide anion was examined. In the presence of 0.5 mol% of the Pd complex and dppf as ligand in NMP, the reaction reached completion at 60°C in 4h to afford benzonitrile in an excellent yield.

KEY WORDS: Aryl Cyanation/ $Pd_2(dba)_3 \cdot CHCl_3$

INTRODUCTION

The inertness of halogens bound to an sp^2 carbon atom prevents a nucleophilic displacement of non-activated aryl halides through the conventional procedures. In certain cases, however, such difficulty is overcome by using a transition-metal complex as exemplified by a pronounced catalysis of nickel or palladium in the reaction between aryl halides and organometallics, amines, thiols and so on.[1] Concerning the reaction of the substrates with cyanide anion, the present author had shown the effectiveness of palladium catalyst: in the presence of a catalytic amount of palladium(II) salt, non-activated aryl halides underwent the nucleophilic displacement with potassium cyanide to afford corresponding aryl cyanides in good yields under mild conditions.[2] Detailed investigations revealed that the palladium(II) salt was initially reduced to a metallic palladium, which played the role of an active catalyst. Another important observation was the inhibitory effect of cyanide anion itself on the catalytic reaction: the reaction proceeded most well in hexamethylphosphoric triamide (HMPA) where potassium cyanide was least dissolved. Subsequently, tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$) had been shown to be effective for the cyanation, too.[3] But the air-sensitive complex was not so reactive and reported catalyst systems were rather complicated: $Pd(PPh_3)_4$-crown ether, -alumina, or -reducing potential.

In the present investigation, we examined the ability of another zero-valent palladium, $Pd_2(dba)_3 \cdot CHCl_3$ (tris(dibenzylideneacetone)(chloroform)-di-palladium(0)).[4] The effects on the reaction process of solvent and the addition of various ligand were examined intending to find convenient and effective catalytic systems for the aryl cyanation.

高木謙太郎 : College of Liberal Arts and Science, Okayama University, Tsushima, Okayama 700.

RESULTS AND DISCUSSION

Effect of Solvent. The reaction of iodobenzene with potassium cyanide was examined in the presence of 0.5 mol% of $Pd_2(dba)_3 \cdot CHCl_3$ in various common solvent at 60°C.[5] As shown in Table 1, in 1-methyl-2-pyrrolidinone (NMP) or tetrahydrofuran (THF) the cyanation

Table 1. Pd (O)-catalyzed Cyanation of Iodobenzene.[a]

Run	Solvent	Ligand	Conversion/%	Yield/%[b] C_6H_5CN
1	AN	—	<1	<1
2	DMF	—	<1	<1
3	THF	—	9	8
4	NMP	—	46	40
5	NMP	PPh_3	<1	<1
6	NMP	PBu_3	<1	<1
7	NMP	dppp	6	5
8	NMP	P(*o*-Tol)$_3$	84	79
9	NMP	dppf	100	97

a) In the presence of 1 mmol of iodobenzene, 2 mmol of potassium cyanide, 0.005 mmol of $Pd_2(dba)_3 \cdot CHCl_3$, and 0.02 or 0.04 mmol of ligand (when used) in 0.5 cm^3 of the solvent at 60°C for 5h (Runs 1–8) or 4h (Run 9) under nitrogen.
b) Yields were determined by GLC using an internal standard.

$$C_6H_5I + KCN \xrightarrow{\text{Pd catalyst}} C_6H_5CN + KI$$

took place. Although the catalytic reaction stopped before it reached completion, benzonitrile was obtained selectively in either solvent (87 or 89% after 40 or 8 turnover). On the other hand, the catalytic reaction did not occur in *N,N*-dimethylformamide (DMF) or acetonitrile (AN). Apparently this remarkable effect of solvents could not be attributable to the simple medium effect (e.g., dielectric constant: AN=37.5, DMF=36.71, NMP=32.0, THF=7.58).[6]

Effect of Ligand. The reaction of iodobenzene with potassium cyanide was examined in the presence of 0.5 mol% of $Pd_2(dba)_3 \cdot CHCl_3$ and 4 mol% of phosphorus or 2 mol% of diphosphorus ligand in NMP at 60°C. As shown in Table 1, such ligand as triphenylphosphine (PPh_3), tributylphosphine (PBu_3), or 1,3-bis(diphenylphosphino)propane (dppp) did not improve the reactivity. Whereas the addition of tri(*o*-tolyl)phosphine (P(*o*-Tol)$_3$) or 1,1′-bis(diphenylphosphino)ferrocene (dppf) gave a favorable catalyst system. Although a clear account of these effects can not be offered at the present stage, the nature of species (including solvent molecules and phosphorus ligands) ligated to palladium(0) did alter its reactivity remarkably.

In conclusion, a new and efficient reaction system, $Pd_2(dba)_3 \cdot CHCl_3$+dppf catalyst in NMP, was developed for aryl cyanation, which might provide a convenient and practical synthetic procedure of aryl cyanides starting from iodoarenes.

EXPERIMENTAL

Materials. $Pd_2(dba)_3 \cdot CHCl_3$ was utilized as obtained from Kanto Chemical Co. Potassium cyanide was recrystallized from water. All the solvents were distilled under nitrogen and stored over Molecular Sieve. The other materials were commercial products and used without further purification.

General Procedure. All the reactions were performed in a test tube equipped with a magnetic stirring bar under nitrogen. A mixture composed of potassium cyanide, iodobenezene, $Pd_2(dba)_3 \cdot CHCl_3$, phosphorus ligand (when used), and solvent was degassed by evacuation and flushed with nitrogen. The mixture was then heated at 60°C for 4–5 h with stirring and shaking with aq. NaCl-ether. The organic layer was subjected to GLC analysis.

REFERENCES

(1) P.W. Jolly, "Nickel Catalyzed Coupling of Organic Halides and Related Reactions," in "Comprehensive Organometallic Chemistry," ed by G. Wilkinson, Pergamon Press, Oxford (1982), Vol. 8, p. 723; B.M. Trost and T.R. Verhoeven, "Organopalladium Compounds in Organic Synthesis and in Catalysis," *ibid.*, p. 799.

(2) K. Takagi, T. Okamoto, Y. Sakakibara, and S. Oka, *Chem. Lett.*, **1973**, 471; K. Takagi, T. Okamoto, Y. Sakakibara, A. Ohno, S. Oka, and N. Hayama, *Bull. Chem. Soc. Jpn.*, **48**, 3298 (1975); *idem, ibid.*, **49**, 3177 (1976).

(3) G.P. Ellis and T.M. Romney-alexander, *Chem. Rev.*, **87**, 779 (1987); N. Sato and M. Suzuki, *J. Heterocyclic Chem.*, **24**, 1371 (1987).

(4) The advantages of this palladium complex over those of $Pd(PPh_3)_4$ are that 1) this air-stable complex needs no care in its handling and 2) the fine-tuning of the activity might be possible through modification of the ligand, since dba is replaced readily with other ligands: K. Moseley and P. Maitlis, *J. Chem. Soc., Dalton Trans.*, **1974**, 169.

(5) A special care is necessary in the handling of HMPA: M. Fieser and L.F. Fieser, "Reagents for Organic Synthesis," Wiley-Interscience Publication, New York (1976), Vol. 6, p. 273.

(6) J.A. Riddick and W.B. Bunger, "Organic Solvents," 3rd ed in "Techniques of Chemistry," ed by A. Weissberger, Wiley-Interscience Publication, New York (1970), Vol. 2, p. 536.